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Findings to date are as follows: (a) Most cells recorded in the mMGN show modulated activity during both the acoustic consitioned stimulus (CS) and the trace interval between the CS and the unconditioned stimulus (UC). (b) Modulation of activity is more likely on CS+ trials than CS- trials and on trials with conditioned responses than on trials without conditioned responses. (c) Differences in modulation of activity is primarily expressed as phasic bursts of firing. These observations are basically consistent with related work in other laboratories that have employed other forms of conditioned behavior and in species besides rabbits. The new information this study provides is that learning related activity occurpies that trace interval.

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February 25, 1993

Dr Genevieve Haddad, Ph D
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Dear Dr. Haddad,

Re: AFOSR 92-NL-033; UMass Account 5-28286

This letter is the *Research Progress and Forecast Report* for the current year's work on AFOSR 92-NL-033, **Adaptive Timing of Conditioned Behavior: Neural Representation and Computation**. It covers the period from August 1, 1992 to the present.

Work Accomplished

The past five months have been devoted primarily to building a new laboratory for behavioral experiments, which should go 'on-line' within the next several weeks. Work on refitting two electrophysiology laboratories is essentially complete. The main focus of rebuilding has been to install new computers and interfaces for experimental control and data acquisition. The new behavioral laboratory is based on a new transducer capable of recording movements of the two eyelids responses from up to eight animals run concurrently. The new laboratories are equipped with digital function generators so that we can precisely control dynamical conditioned stimuli such as pulsating acoustic sinusoids. This capability is a departure from traditional procedures in studies of conditioned responding, which have employed simple on-off events as conditioned stimuli. The new laboratories were largely equipped with funds from the current grant.

During the time that the new laboratory has been under construction, we have been pursuing three lines of experimentation, as follows:

1. Postdoctoral associate Dr. Kevin O'Connor has been recording from single neurons of the medial subnucleus of the medial geniculate nuclei (mMGN) during differential trace conditioning. *He presented his preliminary results at last year's neuroscience meetings in* Anneheim. He is continuing these studies so as to increase the number of anatomically confirmed electrode placements for grater reliability. His findings to date are as follows: (a) Most cells recorded in the mMGN show modulated activity during both the acoustic consi-

tioned stimulus (CS) and the trace interval between the CS and the unconditioned stimulus (US). (b) Modulation of activity is more likely on CS+ trials than CS- trials and on trials with conditioned responses than on trials without conditioned responses. (c) Differences in modulation of activity is primarily expressed as phasic bursts of firing. These observations are basically consistent with related work in other laboratories that have employed other forms of conditioned behavior and in species besides rabbits. The new information this study provides is that learning related activity occupies that trace interval. The mMGN therefore expresses the heretofore hypothetical 'stimulus trace process' assumed by computational models of conditioned response timing such as the Desmond and Moore (1988) tapped delay-line model described in the accompanying reprints.

2. Anatomical studies using WGA-HRP have conducted by Marcy Rosenfield and new graduate student June-Seek Choi. (Choi has a Masters degree from Korea University, where he worked on the effects of lesions of red nucleus on rabbit eye blink conditioning.) This is part of an ongoing effort to clarify patterns of connectivity among crucial circuit elements supporting eye blink conditioning. Rosenfield and Choi have been implanting WGA-HRP loaded micropipettes into the region of cerebellar cortex that is critical for normal expression of the conditioned response, hemispheral lobule VI of Larsell (HVI). Retrograde labelling of neurons that project to HVI is normally seen in precerebellar structures such as the pontine nuclei and inferior olive. The question is interest is whether the red nucleus also sends projections to HVI. The red nucleus has been regarded merely as a relay for motor commands initiated in the cerebellum. It has not been regarded as a source of direct input to cerebellar cortex, although there have been a few reports from one laboratory that such a connection exists. We have previously reported evidence for a sparse connection between red nucleus and HVI, and this impression has been confirmed in the latest experiments. I anticipate this latest work being reported at this year's neuroscience meetings.

3. We have been using one of the electrophysiology laboratories to conduct behavioral experiments while the new behavioral laboratory is being constructed. These experiments constitute a new direction of research designed to assess predictions of various models of conditioned response timing. This new direction of research might best be described as *Conditioned Responding Under Temporal Uncertainty*. The basic protocol involves training with randomly varying CS-US intervals. One experiment has been completed and another is in progress. The CS in these experiments is a 300-sec tone, and the US is a mild 1-msec eye shock. The easiest way to describe these experiments is to introduce some notation. Let W be the size of the temporal window, in milliseconds, after the CS in which the US might occur. Let m be the number of possible alternative CS-US intervals within W, randomly chosen by the computer controlling the experiment. Let ISI define the average CS-US interval in milliseconds. The first experiment set $ISI = 500$ for all animals, but W was systematically

varied; $W = 0, 50, 100, 200, 400$. The corresponding values of m were $m = 1, 25, 50, 100, 200$. Hence, the condition $W = 0$ and $m = 1$ specifies a trace conditioning procedure with a constant CS–US interval of 500 msec. The condition $W = 400$ and $m = 200$ specifies a variable trace conditioning procedure in which the US might occur at any of 200 equally spaced CS–US intervals between 300 and 700 msec. (The sampling rate of the computer was set at 500 Hz. Therefore, m was one half of W, where W is expressed in millieseconds.) In the second experiment, which is in progress, $ISI = 500$ and $W = 400$, but $m = 2, 3, 4, 5$ in equal steps. Hence, with $m = 2$, the CS–US interval switches randomly between 300 and 700 msec. With $m = 5$, the CS–US interval varies randomly among 5 equally spaced steps between 300 and 700 msec (i.e, 300, 400, 500, 600, 700 msec).

These experiments on conditioning under temporal uncertainty provide data important for computational models of conditioned response timing. The response measures of interest are conditioned response initiation latency, time to peak response amplitude, and response duration. These data are taken from 'probe trials' on which the US is omitted. In addition to their relevance to computational models of timing, these indices can be related to measures of performance in other domains of motor control, such as speed-accuracy trade-offs. The results of the first experiment indicate that conditioned response latency is a decreasing function of W, but that time to peak is an increasing function of W. Thus, movement time increases with W in a manner consistent with the Desmond and Moore (1988) computational model. The results of this experiment and the one now in progress will be presented at a symposium entitled *Neurobiology of Learning and Memory Including LTP and LTD* to be convened in Glasgow, Scotland next August as part of the 32nd International Congress of Physiological Sciences. I am one of the featured invited speakers on the program.

Major Equipment

The major equipment purchases under the grant were those described in the original proposal, with one exception. Three thousand dollars originally earmarked for computer interfacing was applied toward the purchase of new transducers for the behavioral laboratory. This alteration of the equipment budget was approved by our grants and contracts administrators.

Commitments of Personnel

There have been some changes in laboratory personnel. Graduate student Michael Hirl will be leaving my laboratory. His place will be taken by Mr. Choi. (I have recruited another graduate student to begin either in the summer or next fall. This is a Ms. Darlene Brunzell who did her undergraduate work at the University of Wisconsin.) Kevin O'Connor and Marcy Rosenfield will remain full time on this project.

Deviations from Research Plan

There are two noteworthy deviations from the original research plan.

1. The first concerns our studies of single-units in the pontine nuclei, which we have terminated. Our preliminary experiments, reported as a 1992 neuroscience abstract, failed to detect conditioning-related activity in this structure. This null finding is consistent with models that assume that the motor program for the conditioned response resides within the cerebellum rather than being relayed to the cerebellum by the pontine nuclei. Consistent with previous studies from this laboratory, many nearby reticular formation cells did evince conditioning related activity.

One purpose of this pontine nuclear study was to find direct evidence for the delay-line timing mechanism assumed by the Desmond and Moore (1988) model. This would have manifested itself as a population of cells with individualistic firing patterns, each with its own latency of response to CS onset indicative of its ordinal position in a delay-line cascade. We observed no such patterns, as individual pontine nuclear cells all responded to CS onset with the same basic short-latency burst.

2. The experiments on conditioning under temporal uncertainty will be expanded to provide evidence on the Desmond and Moore (1988) model. By way of illustration, consider the temporally specific blocking effects predicted by the model. Suppose an animal is initially trained to a tone CS with $W = 0$ and $m = 1$, i.e., traditional training with a fixed CS–US interval. This is Stage 1. It is then switched to a training procedure in which the tone and a new CS, a light, are compounded and training is switched to $W = 400$ and $m = 200$. This is Stage 2. We know from the experiments described above that the conditioned response trained in the first stage will have a shorter movement time than the one trained to the compound CS in the second stage. After the second stage, we would probe with the tone and light presented separately. The model predicts that the response to the tone will show the characteristics of responses trained under temporal uncertainty in Stage 2—shorter latency and greater movement time. The response to the light would show the temporally specific blocking predicted by the model—shorter latency and greater movement time, but with a 'gap' in the temporal region of the first-stage CS–US interval. In other words, the light should show a bimodal response. This prediction follows directly the competitive learning rule assumed by the model.

The response timing profile from experiments with low m, such as in the current set of experiments with randomly varying CS–US intervals noted above, also has implications for the Desmond and Moore (1988) model. The model predicts that conditioned responses will evince as many peaks (up to some limit) as there are CS–US intervals in training. Hence,

with $W = 400$ and $m = 2$, the model predicts a bimodal response with peaks corresponding to the two CS-US intervals the animal can experience, one at 300 msec after CS onset, the other 700 msec after CS onset. With $W = 400$ and $m = 3$, three peaks are predicted, etc. Thus far, these are the patterns we have seen in this type of experiment. Thus, the response conditioned under 'coarsely grained' temporal uncertainty (i.e, large W and low m) is jerky and inefficient, as predicted by the model.

We are greatly interested to know whether these conditioned responses with multiple peaks are related to the firing of single neurons on the cerebellum. We know from previous work in the laboratory that the activity of cells in deep cerebellar nucleus interpositus can be highly predictive of single-peaked conditioned responses. Do individual cerebellar cells also predict responses with multiple peaks? Or is the case that individual cells are correlated with some peaks, but not others. We plan experiments to address is this question because they would provide important insights into how motor programs for adaptive behaviors are organized, a highly charged issue in contemporary work on movement control (see Controversies in Neuroscience I: Movement Control, in *Behavioral and Brain Sciences*, 1992, 15, 603-875).

Cordially,

John Moore

John W. Moore, Ph.D.
Professor of Psychology and
Computer Science

Enclosures: five additional copies

six copies each of the following chapters:

1. Moore, J.W. A mechanism for timing conditioned responses. In F. Macar et al. (eds.), *Time, Action and Cognition*, 229-238, Kluwer Academic Publishers, 1992

2. Moore, J.W. Knowledge structures in temporally adaptive conditioned responding. In L.R. Squires and N. Butters (eds.) *Neuropsychology of Memory, 2nd Edition*, 510-518, The Guilford Press, 1992.

cc to Office of Grants and Contracts (Account 5-28329)